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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/714,333	11/14/2003	Anastasia Khvorova	DHARMA 0100-US2	6379
23719 7590 12/22/2008 KALOW & SPRINGUT LLP 488 MADISON AVENUE 19TH FLOOR NEW YORK, NY 10022				
EXAMINER				
PITRAK, JENNIFER S				
ART UNIT		PAPER NUMBER		
1635				
MAIL DATE		DELIVERY MODE		
12/22/2008		PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/714,333

**Applicant(s)**

KHVOROVA ET AL.

**Examiner**

JENNIFER PITRAK

**Art Unit**

1635

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 20 August 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1, 38-54, 57-66, 68, and 70-91 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 38-54, 57-66, 68 and 70-91 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Remarks***

The Office Action mailed 07/18/2008 was vacated and was replaced by the Office Action mailed 08/22/2008, only to correct errors in the Office Action Summary sheet (page 2). The substance of the 07/18/2008 Office Action and the 08/22/2008 office action were the same. Applicant's response to the 07/18/2008 Office Action was received 08/20/2008. Applicant's response to the 08/22/2008 Office Action was received 09/12/2008 and requested consideration of the arguments presented in Applicant's 08/22/2008 response. The 08/20/2008 arguments will be considered in response to the 08/22/2008 Office Action.

**Claims 1, 38-54, 57-66, 68, and 70-91 are pending and are under examination.**

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### ***Claim Rejections - 35 USC § 101 - New***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 61-66, 68, 70-77, 80, 81, 89, and 91 are rejected under 35 U.S.C. 101 because the claims are directed to non-statutory subject matter.

The instant claims are drawn to methods comprising applying a computer algorithm comprising several criteria to siRNA sequences and outputting an siRNA sequence in a form that is readable by computer. The instant claims require no physical transformation of any matter and

produces no useful, tangible, or concrete final result. Output readable by a computer includes output such as carrier waves, which are natural phenomena and are non-statutory under 35 USC § 101.

***Claim Rejections - 35 USC § 112 Second paragraph - New***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 43-54, 57-60, 79, and 84-87 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are directed to methods for obtaining an siRNA molecule comprising a step of applying a criteria to candidate siRNA sequences that consists of specific nucleotides at specific positions within the **antisense** strand of the siRNA, wherein the positions are defined in reference to the 5'-end of the antisense sequence, not necessarily within the siRNA duplex region. The siRNAs comprise a sense and an antisense sequence, each 19-30 nucleotides in length, wherein the sense and antisense sequences form a duplex region of 19-30 base pairs. Therefore, siRNAs according to the claims may have a 19-base-pair duplex region and from 0-11-nucleotide overhanging ends or a 30-base-pair duplex with 0-nucleotide overhanging ends, for example.

The specification defines positions in an siRNA duplex with reference to the **sense** sequence. For example, the specification at pages 22-23 explains the numbering of positions of the sense sequence. It is understood that the numbering of the antisense sequence is to be the same as that specified for the sense sequence, which is consecutive numbering starting at the 5' end of the antisense strand. However, the positions are not defined relative to either the very 5'-

most-end of the sense or antisense strand or to the 5'-most-base-paired nucleotide in the sense or antisense strand. Therefore, the limitations such as, for example, "the presence of A at position 10 of the antisense sequence," is unclear as to the relative position of the A in the antisense strand. For example, an "A at position 10 of the antisense sequence" may refer to an A in an overhanging nucleotide relative to the very first position of the entire antisense strand sequence or it may refer to an A at position 10 relative to the very first base-paired nucleotide in the antisense strand. The very first position of a strand may or may not be base-paired. In the amendments to the claims filed 12/03/2007, the limitation "within said duplex region" was deleted, thereby creating ambiguity with regard to the claimed nucleotide positions. Therefore, the claims are indefinite.

*Claim Rejections - 35 USC § 112 First paragraph - New*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 38-42, 61-66, 78, 80, 82, 83, and 88-91 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a **new matter** rejection.

The claims are directed to methods for obtaining an siRNA molecule comprising applying a criteria to candidate siRNA sequences consisting of assessing the relative number of A and U nucleotides present in the first 1-5 nucleotide positions at the 5' terminus of the

antisense region compared to that present in the last 1-5 nucleotide positions at the 3' terminus of the antisense region. These limitations were first introduced into the claims in the amendments filed 10/30/2006.

The specification provides support for assessing the A and U content of the last five nucleotides of the 3' terminus of the sense sequence of an siRNA duplex region. However, the specification does not support the limitation of assessing the relative A and U content of the 5' and 3' termini of the duplex region. For example, see page 31, lines 25-35 and page 37, lines 24-35. The A and U content of the last five nucleotides of the 3' terminus of the sense sequence of the duplex region is described as a criterion for assessing siRNA functionality (page 31, lines 25-35; page 37, lines 24-35). In the same part of the specification it is noted that A and U content of the opposite terminal region of the duplex (the 5' terminal five nucleotides of the sense sequence of the duplex region) appears to not correlate with silencing potency (page 37, lines 24-35). However, this disclosure does not support a criterion wherein the A and U content is higher at the 3' terminus of the sense sequence compared to that at the 5' terminus. The disclosure only supports the criterion wherein the A and U content at the 3' end of the sense sequence of the siRNA duplex region is high, for example, having 3 or more A/Us (p. 37 lines 31-34).

***Claim Rejections - 35 USC § 103 - Withdrawn***

The rejection of claims 1, 38-54, 57-66, 68, and 70-91 under 35 U.S.C. 103(a) as being unpatentable over Tuschl, *et al.* (WO02/44321, of record), Elbashir, *et al.* (2002, of record, 09/05/2007 Office Action), and Walton, *et al.* (1999, Biotech. Bioeng., v.65:1-9, abstract only) is withdrawn. Applicant's arguments were persuasive.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JENNIFER PITRAK whose telephone number is (571)270-3061. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Pitrak  
Examiner  
Art Unit 1635

/Tracy Vivlemore/  
Primary Examiner, Art Unit 1635